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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/915,181	07/24/2001	Robert H. Edwards	305T-932610US	5247

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EXAMINER
SHUKLA, RAM R

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 07/22/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/915,181	EDWARDS ET AL.	
	Examin r	Art Unit	
	Ram R. Shukla	1632	

-- The MAILING DATE f this c mmunication appears n the cover sheet with the corresp ndence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-67* is/are pending in the application.

4a) Of the above claim(s) *10,12-15,17,22-37 and 44-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11,16,18-21 and 38-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's election with traverse of the invention of group VI, claims 1, 11 and 16 in Paper No. 13 is acknowledged.

In response to applicants' arguments in paragraph A, claims 2-9 and 18-21 have been included in the groups IV-IX. Additionally, claims 38-43 have been added to groups I-IX and XVI-XXI

In response to applicants' arguments in paragraph B, it is noted that set 4 of the restriction requirement is directed to claims 61-67 and due to an advertent error the wrong claims were put in this group. Claim 61 in this set has been treated as a linking claim.

Applicants arguments in paragraph C that restriction between groups I, IV, VII, II, V, VIII etc. is legally improper is not found persuasive because the methods encompassed by these groups are not species of a genus, rather they are patentably distinct with distinct steps. However, in response to applicants' arguments regarding claim 1, that claim 1 cannot be divided into 14 applications, claim 1 has been treated as a linking claim and therefore, applicants arguments are moot.

In conclusion the restriction requirement as modified is set forth below:

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-10, 13-15, 18-23, 38-43, drawn to a method of screening for an agent that modulates uptake of glutamate into a cell comprising a nucleic acid encoding VGLUT1 by detecting the expression of VGLUT1 at nucleic acid level, classified in class 435, subclass 6.

IV. Claims 1, 2-9, 11, 16, 18-21 and 38-43, drawn to a method of screening for an agent that modulates uptake of glutamate into a cell comprising a nucleic acid encoding VGLUT1 by detecting the

expression of VGLUT1 at protein level, classified in class 435, subclass 7.1.

VII. Claims 1, 2-9, 12, 17-21 and 38-43, drawn to a method of screening for an agent that modulates uptake of glutamate into a cell comprising a nucleic acid encoding VGLUT1 by measuring the activity of VGLUT1, classified in class 435, subclass 4.

X. Claims 24-26, 29, 30-32 and 35, drawn to a method of prescreening for a potential modulator of glutamate transporter activity by directly contacting a nucleic acid encoding VGLUT1 receptor to the agent in vitro and detecting the binding of the agent to the VGLUT1 nucleic acid, classified in class 435, subclass 388.21.

XIII. Claims 24-26 and 33-35, drawn to a method of prescreening for a potential modulator of glutamate transporter activity by directly contacting a VGLUT1 receptor polypeptide to the agent and detecting the binding of the agent to the VGLUT1 polypeptide, classified in class 435, subclass 388.22.

XVI. Claims 24-26, 29, 30-32, 35 and 38-43, drawn to a method of prescreening for a potential modulator of glutamate transporter activity by contacting a cell comprising a nucleic acid encoding VGLUT1 receptor to the agent ex vivo and detecting the binding of the agent to the VGLUT1 nucleic acid, classified in class 435, subclass 7.2.

XIX. Claims 24-26, 33-35 and 38-43, drawn to a method of prescreening for a potential modulator of glutamate transporter activity by contacting a cell comprising a nucleic acid encoding VGLUT1 receptor to the agent ex vivo and detecting the binding of the agent to the VGLUT1 polypeptide, classified in class 435, subclass 7.8.

XXII. Claims 38-50, drawn to a host cell comprising a nucleic acid encoding VGLUT1 receptor, a kit comprising the cell and a method of increasing glutamate transport in a cell by expression of VGLUT1, classified in class 435, subclass 325.

XXV. Claims 51-60, drawn to a knockout mammal comprising a disruption in endogenous VGLUT1 glutamate receptor, classified in class 800, subclass 8.

SET-II

II. Claims 1-10, 13-15, 18-23, 38-43, drawn to drawn to a method of screening for an agent that modulates uptake of glutamate into a cell comprising a nucleic acid encoding VGLUT2 by detecting the expression of VGLUT2 at nucleic acid level, classified in class 435, subclass 6.

V. Claims 1, 2-9, 11, 16, 18-21 and 38-43, drawn to drawn to a method of screening for an agent that modulates uptake of glutamate into a cell comprising a nucleic acid encoding VGLUT2 by detecting the expression of VGLUT2 at protein acid level, classified in class 435, subclass 7.1.

VIII. Claims 1, 2-9, 12, 17-21 and 38-43, drawn to drawn to a method of screening for an agent that modulates uptake of glutamate into a cell comprising a nucleic acid encoding VGLUT2 by measuring the activity of VGLUT2, classified in class 435, subclass 4.

XI. Claims 24-26, 29, 30-32 and 35, drawn to a method of prescreening for a potential modulator of glutamate transporter activity by directly contacting a nucleic acid encoding VGLUT2 receptor to the agent in vitro and detecting the binding of the agent to the VGLUT2 nucleic acid, classified in class 435, subclass 388.21.

XIV. Claims 24-26 and 33-35, drawn to a method of prescreening for a potential modulator of glutamate transporter activity by directly contacting a VGLUT2 receptor polypeptide to the agent and detecting the binding of the agent to the VGLUT2 polypeptide, classified in class 435, subclass 388.22.

XVII. Claims 24-26, 29, 30-32, 35 and 38-43, drawn to a method of prescreening for a potential modulator of glutamate transporter activity by contacting a cell comprising a nucleic acid encoding VGLUT2 receptor to the agent ex vivo and detecting the binding of the agent to the VGLUT2 nucleic acid, classified in class 435, subclass 7.2.

XX. Claims 24-26, 33-35 and 38-43, drawn to a method of prescreening for a potential modulator of glutamate transporter activity by contacting a cell comprising a nucleic acid encoding VGLUT2 receptor to the agent ex vivo and detecting the binding of the agent to the VGLUT2 polypeptide, classified in class 435, subclass 7.8.

XXIII. Claims 38-50, drawn to a host cell comprising a nucleic acid encoding VGLUT2 receptor, a kit comprising the cell and a method of increasing glutamate transport in a cell by expression of VGLUT2, classified in class 435, subclass 325.

XXVI. Claims 51-60, drawn to a knockout mammal comprising a disruption in endogenous VGLUT1 glutamate receptor, classified in class 800, subclass 8.

SET-III

III. Claims 1-10, 13-15, 18-23, 38-43, drawn to drawn to a method of screening for an agent that modulates uptake of glutamate into a cell comprising a nucleic acid encoding VGLUT3 by detecting the expression of VGLUT3 at nucleic acid level, classified in class 435, subclass 6.

VI. Claims 1, 2-9, 11, 16, 18-21 and 38-43, drawn to drawn to a method of screening for an agent that modulates uptake of glutamate into a cell comprising a nucleic acid encoding VGLUT3 by detecting the expression of VGLUT3 at protein level, classified in class 435, subclass 7.1.

IX. Claims 1, 2-9, 12, 17-21 and 38-43, drawn to drawn to a method of screening for an agent that modulates uptake of glutamate into a cell

comprising a nucleic acid encoding VGLUT3 by measuring the activity of VGLUT3, classified in class 435, subclass 4.

XII. Claims 24-26, 29, 30-32 and 35, drawn to a method of prescreening for a potential modulator of glutamate transporter activity by directly contacting a nucleic acid encoding VGLUT3 receptor to the agent in vitro and detecting the binding of the agent to the VGLUT3 nucleic acid, classified in class 435, subclass 388.21.

XV. Claims 24-26 and 33-35, drawn to a method of prescreening for a potential modulator of glutamate transporter activity by directly contacting a VGLUT3 receptor polypeptide to the agent and detecting the binding of the agent to the VGLUT2 polypeptide, classified in class 435, subclass 388.22.

XVIII. Claims 24-26, 29, 30-32, 35 and 38-43, drawn to a method of prescreening for a potential modulator of glutamate transporter activity by contacting a cell comprising a nucleic acid encoding VGLUT3 receptor to the agent ex vivo and detecting the binding of the agent to the VGLUT3 nucleic acid, classified in class 435, subclass 7.2.

XXI. Claims 24-26, 33-35 and 38-43, drawn to a method of prescreening for a potential modulator of glutamate transporter activity by contacting a cell comprising a nucleic acid encoding VGLUT3 receptor to the agent ex vivo and detecting the binding of the agent to the VGLUT3 polypeptide, classified in class 435, subclass 7.8.

XXIV. Claims 38-50, drawn to a host cell comprising a nucleic acid encoding VGLUT3 receptor, a kit comprising the cell and a method of increasing glutamate transport in a cell by expression of VGLUT3, classified in class 435, subclass 325.

XXVII. Claims 51-60, drawn to a knockout mammal comprising a disruption in endogenous VGLUT1 glutamate receptor, classified in class 800, subclass 8.

3. Claim 1 and 38 links inventions of the groups I-IX. The restriction requirement between the linked inventions is subject to the non-allowance of the linking claim(s), claim 1. Upon the allowance of the linking claims, the restriction requirement as to the linked invention shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims or the continuation or divisional application may be subject to provisional statutory and/or non-statutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 USC 121 are no longer applicable. See In re Ziegler, 44 F.2d 1211, 1215, 170 USPQ 129,131-132 (CCPA 1971). See also MPEP 804.01.

SET-IV

XXVIII. Claims 61-67, drawn to a method of increasing or inhibiting glutamate uptake in a cell comprising contacting a cell with an agent that inhibits or increases the expression or activity of a VGLUT polypeptide, wherein said agent is an antisense molecule, classified in class 514, subclass 44.

XXIX. Claims 61-67, drawn to a method of increasing or inhibiting glutamate uptake in a cell comprising contacting a cell with an agent that inhibits or increases the expression or activity of a VGLUT polypeptide, wherein said agent is an ribozyme molecule, classified in class 514, subclass 44.

XXX. Claims 61-67, drawn to a method of increasing or inhibiting glutamate uptake in a cell comprising contacting a cell with an agent that inhibits or increases the expression or activity of a VGLUT polypeptide,

wherein said agent is an catalytic DNA molecule, classified in class 514, subclass 44.

XXXI. Claims 61-67, drawn to a method of increasing or inhibiting glutamate uptake in a cell comprising contacting a cell with an agent that inhibits or increases the expression or activity of a VGLUT polypeptide, wherein said agent is an anti-VGLUT antibody, classified in class 514, subclass 2.

XXXII. Claims 61-67, drawn to a method of increasing or inhibiting glutamate uptake in a cell comprising contacting a cell with an agent that inhibits or increases the expression or activity of a VGLUT polypeptide, wherein said agent is a nucleic acid that disrupts a VGLUT gene by homologous recombination, classified in class 514, subclass 44.

4. Claim 61 links inventions of the groups XXVIII-XXXII. The restriction requirement between the linked inventions is subject to the non-allowance of the linking claim(s), claim 1. Upon the allowance of the linking claims, the restriction requirement as to the linked invention shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims or the continuation or divisional application may be subject to provisional statutory and/or non-statutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 USC 121 are no longer applicable. See In re Ziegler, 44 F.2d 1211, 1215, 170 USPQ 129,131-132 (CCPA 1971). See also MPEP 804.01.

The requirement is still deemed proper and is therefore made FINAL.

5. Claims 10, 12-15, 17, 22-37 and 44-67 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 13.

6. Claims 1, 2-9,11, 16, 18-21 and 38-43 encompassing VGLUT3 and assaying the presence of protein (the invention of group VI) are under consideration. Claim 1 is under consideration as a linking claim for nonallowance.

Information Disclosure Statement

The international search report for PCT/US01/23331 has been considered, however due to the lack of a publication date, it cannot be published in a patent and therefore has been crossed out in the IDS.

The JP document 10099183 A has not bee considered because the document is in Japanese and a translation of the document was not supplied.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1, 2-9,11, 16, 18-21 and 38-43are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because the claimed method does not recite a positive step to relate the preamble of the invention to the recited steps.

Claim 3 is indefinite because it recites the limitation "wherein said lower concentration is the absence of said agent". Since absence of a test agent indicates that no test agent is present, It is unclear as to how absence of agent could indicate presence of the test agent in lower concentrations.

Claims 2, 4-9, 11, 16, 18-21 are indefinite because they depend from claim 1.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 38-40 and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Bellocchio et al (The Journal of Neuroscience 18:8648-8659, 1998).

Bellocchio et al teaches a COS1 cell transfected with BNPI transporter.

Therefore the art anticipates the invention of claim 38-40 and 42.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1, 2-9,11, 16, 18-21, 38-40 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bellocchio et al in view of Hediger et al (US 5,739,284 dated 4-14-1998) or Shashidharan et al (WO 98/11222, 3-19-1998) or JP 10099083, 4-21-1998) and McIntire et al (Nature 389:870-876, 1997) and Conradt et al. J Neurochem. 1997, 68:1244-51.

Bellocchio et al teaches characterization of BNPI transporter, antibody production, transfection of the transporter cDNA in a COS1 cell, western analysis of protein expression and relationship of the transporter and glutamate uptake and glutamatergic transmission. This art does not teach a screening assay for identifying agents that modulate VGLUT uptake in a cell.

The arts, Hediger et al (US 5,739,284 dated 4-14-1998) or Shashidharan et al (WO 98/11222, 3-19-1998) or JP 10099083, 4-21-1998), teach glutamate transporter and methods of screening for compounds that alter glutamate transport (for example, see claim 3 in the Derwent printout for Accession no#1998-289876 for the Japanese document or see section 5.2.4 on page 11-14 of Shashidharan et al). These arts also teach that the compounds that modulate or alter expression of glutamate transporter can be used for treatment of diseases (see Hediger et al, see column 1 or Shashidharan et al, see section 5.3) .

McIntire et al teaches identification and characterization of vesicular GABA transporter in PC12 cells. The art also teaches that these cells contain synaptic-like vesicles (see the second paragraph on page 873).

At the time of the invention, an artisan of skill would have been motivated to modify the methods or cells taught by Bellocchio et al and screen for compounds that modulated the protein level of VGLUT in cells. An artisan would have been motivated to screen for such compounds because such compounds could have potential therapeutic activity for treating neuron related disease conditions. Regarding the claims reciting different types of cells, such as oocytes, it is noted that such cells types are routinely used in experimentation and assays for example, xenopus oocytes are routinely used in experimentations of cellular and membrane

transport. For example, see Conradt et al. J Neurochem. 1997, 68:1244-51 which teaches glutamate/aspartate transporter function in kidney 293 and Xenopus oocytes. Regarding the limitations of excluding different agents in the assay as recited in claims 18-21, it is noted that in a screening assay, using or excluding different compounds based on their structure or function is routine.

14. Claimed invention using VGLUT3 is free of the prior art of record.

15. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. The after-final fax number is (703) 87209307. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the William Phillips whose telephone number is (703) 305-3413.

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER

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PRIMARY EXAMINER

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